ABSTRACTS

Gregory L. Moneta, MD, Abstracts Section Editor

Descending Thoracic Aortic Aneurysm Repair: 12-year Experience Using Distal Aortic Perfusion and Cerebrospinal Fluid Drainage

Estrera AL, Miller CC III, Chen EP, et al. Ann Thorac Surg 2005;80: 1290-6.

Conclusion: There is a low incidence of neurologic morbidity and a relatively low mortality rate following descending thoracic aortic aneurysm repair when distal aortic perfusion and cerebrospinal fluid drainage are routinely utilized.

Summary: The authors sought to document their rate of neurologic deficit and mortality following thoracic aneurysm repair with routine utilization of distal aortic perfusion and cerebrospinal fluid drainage. There were 355 descending thoracic aortic aneurysms repaired at the author's institution between February 1991 and September 2004. Twenty nine patients were excluded from analysis because of involvement of the aortic arch and 26 patients with rupture were also excluded. There were therefore 300 patients analyzed for outcomes. Of these, 198 (66%) were men and 102 (35%) were women. Mean age was 67 years. A combination of distal aortic perfusion and cerebrospinal fluid drainage was utilized in 238 patients. There were 62 patients who underwent simple cross-clamp without utilization of distal aortic perfusion or CSF drainage.

There was a 2.3% incidence of neurologic deficit in this series (7 of 300 patients). The rate of neurologic deficits in the patients treated with cerebrospinal fluid drainage and distal aortic perfusion was 1.3% (3 of 238 patients). The rate of neurologic deficit in patients not treated with cerebrospinal fluid drainage and distal aortic perfusion was 6.5% (4 of 62 patients; $P < 0.02$). Neurologic deficits in both groups were only seen when the aneurysm involved the entire descending thoracic aorta. Predictors of neurologic deficit included use of cerebrospinal fluid drainage and distal aortic perfusion (odds ratio [OR] 0.19; $P = 0.02$), previous repaired abdominal aortic aneurysm (OR, 7.0; $P = 0.005$) and aneurysm that involved the entire descending thoracic aorta (OR 13.73; $P = 0.02$) and a history of cerebrovascular disease (OR 4.7; $P < 0.03$). Thirty-day operative mortality was 8%. Predictors of 30 day mortality were preoperative renal dysfunction (OR, 4.6; $P < 0.01$) and female sex (OR, 2.9; $P < 0.03$).

Comment: This paper from Dr. Safi's group in Houston indicates what is possible to achieve with open thoracic aneurysm repair. I doubt this volume of patients and this level of expertise is present in many institutions. Because of this, papers such as this cannot really be used to justify or not justify endovascular techniques of thoracic aneurysm repair. However, with data such as this it would seem silly not to provide, when possible, CSF drainage and distal aortic perfusion in patients undergoing open descending thoracic aortic aneurysm repair.

MRI vs Helical CT for Endoleak Detection After Endovascular Aneurysm Repair

Pitton NB, Schweitzer H, Herber S, et al. Am J Radiol 2005;185:1275-81.

Conclusion: MRI is far superior to biphasic CT scans for detection of endoleaks following endovascular aneurysm repair.

Summary: There were 99 patients treated with Nitinol based stent grafts between 1998-2003 at the author's institution. Of these 47 were excluded from analysis because they had follow up at another institution or did not agree to undergo both CT and MRI imaging in follow up or had claustrophobia or contrast allergy or poor renal function. Fifty-two patients therefore had follow up data sets that included MRI and contrast enhanced biphasic CT scans performed within 48 hours after stent graft placement and at 3, 6, and 12 months and yearly thereafter. Endoleaks were categorized as the percent of maximum cross sectional aneurysm area ($<3\%$, $>3\% \leq 10\%$, $>10\% \leq 30\%$, or $>30\%$).

There were 252 data sets available for analysis and 141 showed evidence of endoleak. Incidence of Types 1, 2, 3 and complex endoleak were 3.2%, 40.1%, 8.7%, and 4.0%, respectively. Sensitivities for endoleak detection for MRI, biphasic CT, uniphasic arterial CT, and uniphasic late CT were 92.9%, 44.0%, 34.8%, and 38.3%, respectively. Corresponding negative predictive values were 91.7%, 58.4%, 54.7%, and 56.1%. Overall accuracies for MRI, biphasic CT, uniphasic arterial CT, and uniphasic late CT, were 95.2%, 58.3%, 55.6%, and 57.1%, respectively.

Comment: The data clearly implied that endoleak rates after endovascular aneurysm repair are dependent upon the imaging modality utilized to detect the endoleak. MRI appears to detect more endoleaks than CT. It is interesting to speculate whether unexplained endotension after endovascular aneurysm repair essentially reflects undetected endoleak. Perhaps unexplained endotension after endovascular aneurysm repair would be explained far more often if MRI rather than CT was used routinely in the evaluation of endoleaks following endovascular aortic aneurysm repair.

Trends in Serum Lipids and Lipoproteins of Adults 1960-2002

Carroll MD, Lacher DA, Sorlie PD, et al. JAMA 2005;294:1773-81.

Conclusion: Total cholesterol and LDL cholesterol levels show continued decline from 1960-2002 with attainment of the target value of no more than 17% of US adult population of having a total cholesterol level $\geq$240 mg/dl.

Summary: Both total and low density lipoprotein (LDL) cholesterol levels have been followed by the National Health and Nutrition Examination Surveys (NHANES) from 1960-2002. Overall both total and LDL cholesterol levels have tended to decrease. This study focused on changes in LDL and total cholesterol levels since the previous NHANES survey from 1988-1994. Blood lipid measurements were examined in 5 cross-sectional surveys in the US population during the periods 1960-1962, 1971-1974, 1976-1980, 1988-1994, 1999-2002. Mean serum total cholesterol, LDL cholesterol, high density lipoprotein (HDL) cholesterol and mean serum triglyceride levels and the percentage of adults with a total serum cholesterol $>$240 mg/dl were determined. There were from 6,000 in 1998 to 15,019 adults examined in the 5 district cross-sectional surveys.

Between 1988-1994 and 1999-2002 total cholesterol level of 20 years or older adults decreased from 206 mg/dl to 203 mg/dl ($P = 0.009$). LDL cholesterol levels decreased from 129 mg/dl to 123 mg/dl ($P < 0.001$). Men who are $>$60 years of age had more significant decreases than women $>$50 years of age. Overall, the percentage of adults with a total cholesterol level 240 mg/dl decreased from 20% during the period of 1988-1984 to 17% during the period of 1999-2002 ($P < 0.001$). Mean HDL levels did not change and there was a nonsignificant increase in mean serum triglycerides ($P = 0.06$).

Comment: The data indicate continued and sustained progress in reducing cholesterol levels in the US population. Now only 17% of the US adult population has a total cholesterol level 240 mg/dl. Clearly there is still room for improvement and further analyses targeting the ability to reduce cholesterol levels in patients particularly at high risk for coronary disease and other forms of vascular disease is required.

Secondary Prevention of Macro Vascular Events in Patients With Type II Diabetes in the PROactive Study (PROspective Pioglitazone Clinical Trial and Macro Vascular Events): A Randomised Controlled Trial

Dormandy JA, Charbonnel B, Eckland DJA, et al. Lancet 2005;366:1279-89.

Conclusion: In patients with Type II diabetes felt to be at high risk for macro vascular events, Pioglitazone reduces the combination of all cause mortality, non fatal myocardial infarction, and stroke.

Summary: This study sought to evaluate the effects of an antagonist of peroxisome proliferator-activated receptor gamma for its ability to reduce macro vascular complications in patients with Type II diabetes. This was a prospective, randomized control trial involving 5,238 patients with Type II diabetes and who had evidence of macro vascular disease. Patients were recruited from both hospitals and primary care practices. Patients were divided into two groups with one group treated with a titrated dose of pioglitazone from 15 mgs to 45 mgs (n = 2,605) with the second group being a placebo control (n = 2,603) study. Medications in both groups were taken in addition to glucose lowering drugs and other indicated medications. The primary end point in the study was a composite of all cause mortality, non fatal myocardial infarction, stroke, acute coronary syndrome, and endovascular or surgical intervention in the coronary or leg arteries, or amputation above the ankle. An intention to treat analysis was utilized.

There were only two patients lost to followup in this study. Average observation time was 34.5 months. In the pioglitazone group, 514 patients had at least one event in the primary composite end point versus 572 patients in the placebo group (hazard ratio 0.9, 95% CI, 0.8-1.02, $P = 0.095$). With regard to the combination of all cause morality, non fatal myocardial infarction, and stroke, 301 patients in the Pioglitazone group and 358 patients in the placebo group achieved this end point (hazard ratio 0.84, 95% CI, 0.72-0.98, $P = 0.027$). There was no change in the safety profile of Pioglitazone noted. During the course of the study, 6% of the patients in the Pioglitazone group and 4% in the placebo group were admitted to the hospital with heart failure. There was no difference in mortality rates from heart failure between the two groups.

Comment: Pioglitazone reduces levels of inflammatory markers such as C-reactive protein. These effects are independent of its affect on glycemic

control. Detailed analysis of the data indicates the drug had no effect on leg revascularization or need for amputation. There is beginning to be accumulated evidence that systemic markers of inflammation are perhaps more important in predicting coronary events than events secondary to peripheral vascular disease. If this proves to be true, then the results of this study would make sense in that one of the primary effects of this drug is to lower markers of systemic inflammation.

Increased Platelet Count and Leukocyte-Platelet Complex Formation in Acute Symptomatic Compared With Asymptomatic Severe Carotid Stenosis

McCabe DJH, Harrison P, Mackie IJ, et al. Journal Neurology, Neurosurgery, Psychiatry 2005;76:1249-54.

Conclusion: The mechanism of symptomatic carotid stenosis predisposing to stroke may in part be related to increased platelet count and leukocyte-platelet complex formation.

Summary: The authors sought to determine why risk of stroke is significantly higher in patients with recently symptomatic carotid stenosis versus those with asymptomatic carotid stenosis. They hypothesized that excess platelet activation may contribute to this difference. Patients were tested with whole blood flow cytometry to measure platelet surface expression of CD62P, CD63, and PAC1 binding and percentage of leukocyte platelet complexes. Three groups of patients were evaluated. Those who had acute symptoms in the previous 0-21 days (n = 19), convalescent patients who had symptoms from 79-365 days in the past (n = 16), and patients with asymptomatic carotid stenosis (n = 16). Most patients were on aspirin, although alternative anti-thrombotic therapies were used more often in the patients with symptomatic carotid stenosis.

In patients with acute and convalescent symptomatic carotid stenosis, the mean platelet count was higher than in patients with asymptomatic carotid stenosis. There were no differences between CD62P, CD63, or PAC1 binding between the three groups. Patients with acute symptomatic carotid stenosis had higher median percentages of neutrophil-platelet, monocyte-platelet, and lymphocyte-platelet complexes (p, 0.004, 0.046, and 0.02 respectively). In patients on only aspirin therapy, neutrophil platelet and monocyte platelet complexes were higher in those with acute symptomatic plaques than in patients with asymptomatic plaques (P = 0.03). In patients with convalescent symptomatic carotid stenosis, median percentages of leukocyte platelet complexes in the symptomatic group were similar to those found in the asymptomatic group.

Comment: The severity of carotid stenosis appears to be reasonably well correlated with symptoms in symptomatic patients and perhaps moderately well correlated in asymptomatic patients. Nevertheless, most patients with even severe carotid stenosis do not have strokes. Much research has focused on the plaque as a discerning factor for risk of stroke in patients with carotid stenosis. Research such as this presented here is also highly interesting in that it suggests the risk of stroke is going to be effected not only by stenosis and plaque composition, but also by blood rheology.

Association of a Functional Polymorphism in the Clopidogrel Target Receptor Gene P2Y12 and the Risk for Ischemic Cerebrovascular Events in Patients With Peripheral Arterial Disease

Ziegler S, Schillinger M, Funk M, et al. Stroke 2005;36:1394-9.

Conclusion: There is a variable response to Clopidogrel in patients with peripheral arterial disease (PAD). This may lead to an increase in cerebrovascular events.

Summary: Clopidogrel is an antiplatelet agent with considerable variability in antiplatelet affects. Clopidogrel resistance has been shown to be associated with recurrent cardiovascular events in patients with acute coronary syndromes. The authors assessed the effect of gene sequence variations in P2Y12 with occurrence of neurologic adverse events in patients with symptomatic PAD who were treated with clopidogrel. Patients who had symptomatic PAD as manifested by intermittent claudication, critical limb ischemia, or a history of surgical or endovascular lower limb revascularization were eligible for the study. There were 137 patients who were undergoing antiplatelet therapy with clopidogrel and 336 who were treated with aspirin. These patients were followed for occurrence of neurologic events (ischemic stroke and/or carotid revascularization). Polymerase chain reaction was used to determine the prevalence of 2 polymorphisms of the P2Y12 gene, 34C>T and 52G>T.

Mutated, heterozygous and wild type alleles for the 34 C>T polymorphism were 9% (n = 40), 44% (n = 210), and 47% (n = 223). Genotype frequencies for the mutated, heterozygous and wild type alleles for the 52G>T polymorphism were 4% (n = 17), 27% (n = 127), and 70% (n = 329). Median followup was 21 months. Eight percent of the patients had a neurologic event during followup. Patients treated with aspirin showed no association between neurologic events and either the 34C>T or 52G>T polymorphisms. However, clopidogrel patients with at least one 34T allele had a 4.02 times increased risk for neurologic events compared with carriers of only 34C alleles (95% confidence interval, 1.08 to 14.9).

Comment: Like with aspirin, there appears to be a significant inter-individual variability in the antiplatelet effect of clopidogrel. This study suggests identification of the 34C>T polymorphism may serve as a predictor of the efficacy of clopidogrel to prevent neurologic events in patients with PAD. Patients with neurologic events on antiplatelet therapy should probably be assessed for either aspirin or clopidogrel resistance, and their antiplatelet agent adjusted accordingly.

Statins are Associated with Better Outcomes After Carotid Endarterectomy in Symptomatic Patients

Kennedy J, Kuan H, Buchan AM, et al. Stroke 2005;36:2073-6.

Conclusion: Statin therapy appears to have a protective effect in symptomatic patients undergoing carotid endarterectomy.

Summary: Pleiotropic effects of statins are widely appreciated. Statins are associated with a reduction in mortality in non cardiac surgery. This study determined the effect of statin use at the time of hospital admission in patients undergoing carotid endarterectomy. The authors sought to determine whether statin use at the time of hospital admission in patients undergoing carotid endarterectomy was associated with a reduction of in-hospital adverse outcomes. All carotid endarterectomy cases were identified in four western Canadian provinces from January 2000 to December 2001. Charts were abstracted for data describing patient characteristics, surgical indication for endarterectomy, statin treatment, and in-hospital outcomes with respect to death, ischemic stroke, as well as cardiac outcomes. There were 3,360 patients included in the data base. Logistic regression analysis was used to compare outcomes of patients on statins versus those not on statins and to account for differences in patient characteristics. Propensity score analysis was used to account for factors that may influence patient treatment with statins.

At the time of hospital admission, 815 of 2,031 symptomatic patients and 665 of 1,252 asymptomatic patients were on a statin medication. Symptomatic patients on statins had reduced in-hospital mortality and in-hospital ischemic stroke and death rates. There was no difference in in-hospital cardiac outcomes. (Adjusted odd ratios 0.25 {CI, 0.07 to 0.90}, 0.55 {CI, 0.32 to 0.95}, 0.87 {CI, 0.49 to 1.54}, respectively). Improvement in outcome of symptomatic patients was robust when tested with propensity score analysis. The association between outcomes and statin use was not seen in asymptomatic patients.

Comment: The study adds to the growing impression that statins improve perioperative outcomes in patients undergoing vascular surgery. The lack of effect of statins in the asymptomatic patients undergoing carotid endarterectomy may be the result of an inability to detect the statin effect due to the low frequency of adverse events in the asymptomatic patients. Since this was not a randomized study, statins, however, may just be serving as a marker of overall better perioperative care. Results of this observational study and others like it will need to be confirmed in large multi-center randomized trials specifically addressing perioperative use of statins to improve operative outcomes.

Relationship Between HbA_{1c} Level and Peripheral Arterial Disease

Munter P, Wildman RP, Reynolds K, et al. Diabetes Care 2005;28:1981-7.

Conclusion: There is an association between higher levels of hemoglobin A_{1c} and peripheral arterial disease, even in patients without diabetes.

Summary: Glucose control is felt to be important in the development of peripheral arterial disease (PAD) in patients with diabetes. Glucose control may also be important in the development of PAD in patients without diabetes. The authors sought to evaluate hemoglobin A_{1c} levels in patients with and without diabetes and to compare these levels with prevalence of PAD.

This was a cross sectional study utilizing 4,526 participants in the National Health and Nutrition Examination Survey, 1999-2002. Participants were all >40 years of age. PAD was defined as the presence of an ankle brachial index (ABI) <0.9 (n = 327).

In patients without diabetes, age standardized prevalence of PAD was 3.1%, 4.8%, 4.7%, and 6.4% for subjects with a hemoglobin A_{1c} <5.3%, 5.3-5.4%, 5.5-5.6%, and 5.7-6.0%, respectively (p-trend less than 0.001). In patients with diabetes, peripheral arterial disease prevalence was 7.5% and 8.8% with respect to hemoglobin A_{1c} levels <7% and ≥7%. Using multivariable analysis adjustments in comparison with non diabetic subjects, with hemoglobin A_{1c} less than 5.3%, the odds ratio (95% confidence intervals) of PAD for diabetic subjects with hemoglobin A_{1c} 5.3-5.4%, 5.5-5.6%, and 5.7-6.0% was 1.41 (0.85-2.32), 1.39 (0.70-2.75), and 1.57 (1.02-2.47) respectively. The odds ratios for peripheral arterial disease in diabetic participants with hemoglobin A_{1c} levels <7% versus those >7% were 2.33 (1.15-4.70), and 2.74 (1.25-.02) respectively.

Comment: The data suggests higher levels of hemoglobin A_{1c} in patients without diabetes may serve as a marker for increased risk of subclinical cardiovascular disease. It may be that it's not so much diabetes but glucose control that contributes to the risk of atherosclerosis. Perhaps diabetes merely serves as one end of the spectrum of the adverse effects of increased glucose levels on atherosclerosis.